Supplementary Methods

In vitro Parallel artificial membrane permeability assay (PAMPA).

Prediction of the brain penetration was evaluated using a parallel artificial membrane permeability assay (PAMPA). Ten commercial drugs, phosphate buffer saline solution at pH 7.4 (PBS), EtOH and dodecane were purchased from Sigma, Across organics, Aldrich and Fluka. The porcine polar brain lipid (PBL) (catalog no. 141101) was from Avanti Polar Lipids. The donor plate was a 96-well filtrate plate (Multiscreen® IP Sterile Plate PDVF membrane, pore size is 0.45 μM, catalog no. MAIPS4510) and the acceptor plate was an indented 96-well plate (Multiscreen®, catalog no. MAMCS9610) both from Millipore. Filter PDVF membrane units (diameter 30 mm, pore size 0.45 μm) from Symta were used to filter the samples. A 96-well plate UV reader (Thermoscientific, Multiskan spectrum) was used for the UV measurements. Test compounds: 3-5 mg of Cafeine, Enoxacine, Hydrocortisone, Desipramine, Ofloxacine, Piroxicam, Testosterone, 12 mg of Promazine and 25 mg of Verapamile and Atenolol, were dissolved in EtOH (1000 μL). 100 μL of this compound stock solution was taken 1400 μL of EtOH and 3500 μL of PBS pH=7.4 buffer were added to reach 30% of EtOH concentration in the experiment. These solutions were filtered. The acceptor 96-well microplate was filled with 180 μL of PBS/EtOH (70/30). The donor 96-well plate was coated with 4 μL of porcine brain lipid in dodecane (20 mg mL^{-1}) and after 5 minutes, 180 μL of each compound solution was added. 0.25mg of SC001 compound was dissolved in 1500 μL of EtOH and 3500 μL of PBS pH=7.4 buffer and then added to the donor 96-well plate. Then the donor plate was carefully put on the acceptor plate to form a "sandwich", which was left undisturbed for 2h and 30 min at 30 °C. During this time the compounds diffused from the donor plate through the brain lipid membrane into the acceptor plate. After incubation, the donor plate was removed. The concentration of compound SC001 and commercial drugs in the acceptor and the donor wells was determined by UV plate reader. Every sample was analyzed at three to five wavelengths, in three wells and in two independent runs. Results are given as the mean [standard deviation (SD)] and the average of the two runs is reported. Ten quality control compounds (previously mentioned) of known BBB permeability were included in each experiment to validate the analysis set.